Nov. 30, 1947.

Dear Frabcis,

Since my last letter, I have been able to accumulate facilities to get some research under way again so that I may in time be able to report work rather than hopes.

The most startling thing I've heard in many a day is in a letter from Evelyn Witkin remarking on the mutagenic potency of NaCl! Have you heard of this? She also mentioned that she planned to study the induction of reverse-mutation at biochemical loci by her melange of mutagens. You may also hear from a fellow, name of Ben Rubin, now at Brookhaven, who got his PhD at Yale last year, who seems to be planning the same sort of thing with radiations. Have you heard from either of them? Acodng Evelyn, the variance of spontaneous reverse-mutations in coli B/r is large as expected.

I am very anxious to hear from you all, and I miss the intellectual stimulations of our discourse. There is a good bunch of minds on this campus, but in a way it is too diversified, too far removed from what I am doing so there is noone who can check very well on my own imagina - tions. How about your, Kim's and Dave's progress? Perk' may be interested to hear that a man named Thurimalakmr in Plant Pathology here has succeeded in carrying certain smuts (Sphacelotheca spp.) through the sexual cycle in vitro culture. We are getting together in trying to lay the groundwork of a genetic investigation which we hope we can entice some new graduate student here into entering.

I spent some time for a while at obtaining some more lactose-and maltose negative mutants in K-12. For some runs I irradiated cell suspensions on the EMB indicator plates. The result was sectored colonies containing both Lac+ and Lac- cells. I am trying to determine whether more than one allele (re mutability of effect on other substrates) can be demonstrated in a given colony in order to discriminate between delayed effects and simple segregation.

Perhaps my closest, and for a variety of reasons today most discouraging interests now are in a study of genetic control of carbohydrases. There seems to be a relationship between ability to utilize lactose and beta-phenyl galactoside, but it is more complex than I first thought. I am having some trouble with quantitative differences between various strains, but I don't know yet whether the basis is multiple allelism or modifiers. The latter would be interesting for its bearing on the 1:1 theory, but I have no simple scheme yet. Most troublesome, the world supply of the synthetic substrate, a gift from Snell, is very limited, and I am near the end of it and no prospect of being able to replenish it for some months.

Among the new mutants are some which are maltose negative in a lactose-negative stock (Y53), which is therefore: T-L-B_1-Lac-Mal-. If you do get on to reversion studies, I would recommend the Lac mutation, which can be studied very nicely on synthetic medium by supplying lactose .01-.05% as sole carbon source. (The growth factor supplements do not interfere The reversions can be seen as papillae in a definite fraction of the tiny Lac- colonies which form if an additional substrate, such as inadvertent hydrolysate of autoclaved lactose is added to support them. I tried to

do the same sort of thing for the T- and the L- reversions on limiting media but did not get very encouraging results. It needs some fooling with however. A further advantage of the Lac locus is that I do have quite a few independent recurrences of it, and that populations heterogeneous for it can be assayed very readily on EMB medium. One of the Lac- mutations may show a selective differential. It (W-30) was represented among more than 50% (!) of the colonies from a previously mustarded population, subsequently incubated 24 hrs. There were not simply only 2 survivors of the mustards treatment. I haven't been able to verify the selective explanation yet, but it seems the only sane one.

Quite a few reversions of Lac- to Lac+ have been tested for their stability re the Lac+ = Lac- mutation, but there was no indication that any of the reversions was unstable at all.

Transformation studies are somewhat in abeyance until various equipment arrives, but they are getting under way with testing stocks, looking for new mutants, etc,

Give our best to Benny, Lillian, etc. Are you coming to Chi for the AAAS meetings? Demerec has quite a schedule set up, Burkholder's has fallen through; There will be a Sonneborn however.

Let's hear from you?,

Sincerely,

Joshua.

F.J.Ryan